PATENT COOPERATION TREATY

# PCT



# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference RLL-338WO | **FOR FURTHER ACTION** | See Form PCT/IPEA/416 |
|---|---|---|
| International application No. PCT/IB2004/000536 | International filing date *(day/month/year)* 01.03.2004 | Priority date *(day/month/year)* 28.02.2003 |
| International Patent Classification (IPC) or national classification and IPC A61K9/20, A61K9/30, A61K31/4439 | | |
| Applicant RANBAXY LABORATORIES LIMITED et al. | | |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the opinion |
| ☐ | Box No. II | Priority |
| ☐ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☒ | Box No. VII | Certain defects in the international application |
| ☐ | Box No. VIII | Certain observations on the international application |

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 23.12.2004 | 08.04.2005 |
| Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Hedegaard, A Telephone No. +49 89 2399-8644 |

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/000536

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   **Description, Pages**

   1-12 as originally filed

   **Claims, Numbers**

   1-39 received on 03.01.2005 with letter of 23.12.2004

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-3, 5-7,10,13-14.17-18,21,23-26,29,31-33,36-37,39 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | 1-3, 5-7,10,13-14.17-18,21,23-26,29,31-33,36-37,39 |
| | No: | Claims | |
| Industrial applicability (IA) | Yes: | Claims | 1-3, 5-7,10,13-14.17-18,21,23-26,29,31-33,36-37,39 |
| | No: | Claims | |

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**Box No. VII Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**Re Item V.**

1 The following documents are referred to in this communication:
D1 : EP 1 004 305 A
D2 : WO 98/52564 A

Document D1 (see Table III) discloses stable preparations comprising a core including sodium rabeprazole (50 mg) and HPC (450 mg).

Document D2 (see example 3) discloses cores including and active drug and small amounts of low viscosity HPC (HPC-L Klucel). On p. 4, l. 4 pariprazole (= rabeprazole) is disclosed as an example of an active drug.

2 The subject-matter of claims 1-3, 5-7, 10, 13-14, 17-18 and 21 (composition); 23-26, 29, 31-33 and 36 (process); and 37 and 39 (method) is novel (Art. 33(2) PCT) since a core comprising rabeprazole and at least 10% w/w of low viscosity HPC has not been disclosed in any of the available prior art documents.

3 The subject-matter of claim 1 differs from D1 (see above under item 1) in that it selects a particular HPC, namely low viscosity HPC.

There is no hint in D1 (alone or in combination with any other document) that more stable compositions of rabeprazole can be obtained when including at least 10% w/w of low viscosity HPC in the core. Therefore, the subject-matter of claims 1-3, 5-7, 10, 13-14, 17-18, 21, 23-26, 29, 31-33, 36-37 and 39 is considered to involve an inventive step (Art. 33(3) PCT).

**Re Item VII.**

1 The claims should be renumbered.

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WE CLAIM:

1. A stable pharmaceutical composition comprising a core, wherein the core includes rabeprazole and at least 10% w/w of low viscosity hydroxypropylcellulose.

2. The stable pharmaceutical composition according to claim 1, wherein the core further comprises an antioxidant.

3. The stable pharmaceutical composition according to claim 1, wherein the viscosity of the low viscosity hydroxypropylcellulose ranges from about 5 m. Pas to about 300 m. Pas.

**4. Cancelled**

**5. Amended.** The stable pharmaceutical composition according to claim 2, wherein the antioxidant comprises one or both of butylated hydroxy toluene and butylated hydroxy anisole.

6. The stable pharmaceutical composition according to claim 5, wherein the antioxidant comprises from about 0.02% to about 0.2% by weight of the total core weight.

7. The stable pharmaceutical composition according to claim 1, wherein the core further comprise polyvinylpyrrolidone.

**8. Cancelled**

**9. Cancelled.**

10. The stable pharmaceutical composition according to claim 7, wherein the polyvinylpyrrolidone comprises from about 0.5% to about 5% by weight of the total core weight.

**11. Cancelled.**

**12. Cancelled.**

13. The stable pharmaceutical composition according to claim 1, wherein the core is coated with a subcoat layer and an enteric coat layer.

**14. Amended.** The stable pharmaceutical composition according to claim 13, wherein the subcoat layer comprises one or more film forming agents comprising one or more of carageenan, ethylcellulose, hydroxypropyl methylcellulose, hydroxypropyl

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cellulose, methylcellulose, carboxymethylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, polyethylene glycol, polyvinyl alcohol and xanthan gum.

**15. Cancelled**

**16. Cancelled.**

**17. Amended.** The stable pharmaceutical composition according to claim 13, wherein the subcoat layer includes an antioxidant.

**18. Amended.** The stable pharmaceutical composition according to claim 13, wherein the enteric coat layer comprises one or more enteric polymers comprising one or more of cellulose acetate phthalate, hydroxypropyl methylcellulose acetate phthalate, polyvinyl acetate phthalate, hydroxy propyl phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate; and methacrylic acid copolymers.

**19. Cancelled**

**20. Cancelled.**

**21. Amended.** The stable pharmaceutical composition according to claim 13, wherein one or more of the core, the subcoat layer, and the enteric layer further comprise pharmaceutically acceptable inert excipients selected from the group consisting of binders, disintegrants, lubricants, glidants, diluents, plasticizers, opacifiers, and coloring agents.

**22. Cancelled**

23. A process for preparing a stable pharmaceutical composition comprising a core, the process comprising:

preparing a core by

(i) blending rabeprazole and a low viscosity hydroxypropylcellulose to form a blend, and

one or both of (ii) granulating the blend and (iii) compressing the blend to form a compact mass core, wherein the low viscosity hydroxypropylcellulose comprises at least 10% w/w of the core.

**24. Amended.** The process according to claim 23, further comprising coating the core with one or both of a subcoat layer and an enteric coat layer.

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25. **Amended.** The process according to claim 23, further comprising blending one or more antioxidants with the rabeprazole and low viscosity hydroxypropylcellulose.

26. The process according to claim 25, wherein the antioxidant is adsorbed over a diluent.

27. **Cancelled.**

28. **Cancelled.**

29. The process according to claim 23, wherein the core is prepared by one or more of a wet granulation method, a dry granulation method, or a direct compression method.

30. **Cancelled.**

31. The process according to claim 24, wherein one or both of the subcoat layer and the enteric coat layer are applied as a solution/suspension.

32. The process according to claim 31, wherein the solution/suspension is prepared in solvents selected from the group consisting of methylene chloride, isopropyl alcohol, acetone, methanol, ethanol, water and mixtures thereof.

33. The process according to claim 24, wherein one or both of the subcoat layer and the enteric coat layer are applied using a hot melt technique.

34. **Cancelled.**

35. **Cancelled.**

36. The process according to claim 24, wherein the viscosity of the low viscosity hydroxypropylcellulose ranges from about 5 m. Pas to about 300 m. Pas.

37. **Amended.** A method of treating digestive ulcers in a mammal by administering to the mammal a stable pharmaceutical composition of rabeprazole according to claim 1.

38. **Cancelled**

39. The method of treating of claim 37, wherein the core further comprises an antioxidant.